The antibody is found in 94 percent of patients with primary biliary cirrhosis, often in very high titers and in 25 to 30 percent of patients with active chronic hepatitis and cryptogenic cirrhosis. The level of antimitochondrial antibody in the serum in primary biliary cirrhosis may vary from trace amounts to titers of 1:6000 and does not correlate with the severity or duration of the disease.

The test is helpful in differentiation of surgical and non-surgical cases of obstructive jaundice since mitochondrial antibody is usually absent in jaundiced patients with extra-hepatic obstructions, drug sensitivity or viral hepatitis. In patients developing jaundice due to chlorpromazine and halothane sensitivity, a low titer of mitochondrial antibody may be seen and disappear upon recovery. The antibody is usually absent in alcoholic cirrhosis.

Mitochondrial antibody of low titer was found in 51 percent of patients showing chronic false positive reactions for syphilis in the absence of detectable liver abnormalities. It is likely that the association of chronic false positive reactions for syphilis and the presence of mitochondrial antibody is associated in a select group of patients with a particular sort of collagen or autoimmune disease.

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Significance of Smooth Muscle Antibodies in Liver Disease

Smooth muscle antibody can be detected in serum samples in the clinical laboratory. This antibody is found mainly in active chronic hepatitis, primary biliary cirrhosis, cryptogenic cirrhosis and present in less than 2 percent of normal subjects. The smooth muscle antibody test is helpful in differentiating active chronic hepatitis from systemic lupus erythematosus (SLE) as smooth muscle antibody is not usually seen in SLE, whereas a positive LE cell test may be observed in both SLE and active chronic hepatitis. The role of smooth muscle antibody in the pathogenesis of chronic liver disease is unknown.

Recently, smooth muscle antibody has been found in cases of acute viral hepatitis. Highest titers were observed during the first month after onset of symptoms. The smooth muscle antibody is most likely related to liver cell damage. No definite correlation between the antibody and hepatitis associated antigen was noted.

Serum IgG and IgM anti smooth muscle antibodies have been reported in 21 percent of patients with intrinsic asthma contrasted with a much lower incidence in extrinsic asthma and chronic bronchitis. The pattern of immunofluorescence observed in cases from intrinsic asthma is distinct from that commonly seen in patients with lever disease.

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Molecular Basis for a Simple, Specific Test for S Hemoglobin: The Murayama Test And Desickling of Sickle Cells with Urea

The Murayama test, a new specific test for S hemoglobin, is based on the molecular mechanism of sickling for S hemoglobin proposed by Murayama. The test depends on a feature of molecular structure: hydrophobic bonds formed between interacting tetramers by the No. 6 valine, which is substituted for glutamic acid near the N-terminal end of each β S globin chain. Ex-

istence of these particular hydrophobic bonds is manifested in deoxygenated, concentrated hemolysates by reversible sol-gel transformations at 0° and 37°C. Deoxygenated hemolysates of S hemoglobin gel at 37°C and liquefy at 0°C. In such systems, demonstration of reversible, temperature-dependent sol-gel transformations (a negative temperature coefficient of gelation is specific for S hemoglobin or the S structural variant, hemoglobin C (Harlem). The test is simple, has clear end-points, will detect both homozygous and heterozygous S hemoglobin, and is specific.

The molecular mechanism for sickling of hemoglobin S has been so precisely defined by the Murayama hypothesis that by extension we have selected on theoretical grounds urea as a chemical desickling agent. Urea attacks intertetrameric hydrophobic bonds implicated by Murayama to break those specific pathogenetic bonds formed in part by the substituted valine residues. Urea forms new hydrophobic bonds of its own with the improperly structured hemoglobin S tetramer, altering the steric structure of the hemoglobin S molecule WITHOUT adversely affecting the vital function of oxygen transport. Thus, by chemical manipulation, a lethal molecular property is inhibited by steric hindrance with the formation of urea-hemoglobin complex, since tetrameric polymerization or "stacking," that is, sickling, is impossible.

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Value of Histochemistry in the Investigation of Human Muscle Diseases

Awareness of the value of histochemical techniques in the investigation of human neuromuscular disorders has increased in the last few years. Such studies have allowed the definition of two or more fiber types, recognition of abnormalities in the reactivity and localization of biochemically defined organelles, determination of the magnitude of collateral reinnervation from type-specific fiber grouping and precise identification of regenerative activity and inflammation.

With such procedures, significant advances have been made in our understanding of the identification and pathogenesis of unusual muscle disorders including nemaline, central core, myotubular and vacuolar myopathy. Increased use of morphometric analysis of fiber types has proved of prognostic and therapeutic value. Newer approaches have placed emphasis on the recognition of the differential susceptibility of fiber types to degeneration or atrophy in a variety of neurogenic and myopathic disorders. Further advances in the recognition and investigation of myopathies will require the continued association of clinician and pathologist.

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Prenatal Diagnosis of Inherited Diseases

A specimen of amniotic fluid (about 10 ml) taken between the 14th and 16th week of pregnancy contains viable cells of fetal origin. The sex of the fetus, chromosomal abnormalities and certain enzyme defects can be diagnosed from these cells after two to four weeks in cell culture. The combined maternal and fetal risk of amniocentesis (probably less than 1 percent) is substantially less than the risk of giving birth to an affected child in families at risk for a detectable genetic disorder (25 percent) or in pregnancies occurring in women over 40 years of age (3 percent). The procedure is not universally applicable, however; not all genetic diseases, and none of the dominant or polygenically inherited disorders, can be detected. The